REMARKS

Claims 50-63 and 65-69 are pending in this application. Claims 66-69 have been withdrawn by the Examiner as being drawn to non-elected inventions. Claims 50-63 and 65 are being considered on the merits.

Claims 51 and 58 have been amended to clarify the present invention. No new matter has been added.

I. THE CLAIM REJECTIONS UNDER 35 U.S.C. § 102 SHOULD BE WITHDRAWN

Claims 50-60 and 65 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Abatangelo *et al.* (WO 97/18842, "Abatangelo"). Specifically, the Examiner alleges that "while applicant argues the structures are materially different,...applicant has neither disclosed how the structures are materially different nor provided any evidence supporting that the structures are materially different." (see Office Action, page 3, ¶4). For the following reasons, Applicant respectfully disagrees.

1. The Legal Standard

An anticipating reference must describe and enable the claimed invention, including all the claim limitations, with sufficient clarity and detail to establish that the subject matter already existed in the prior art and that its existence was recognized by persons of ordinary skill in the field of the invention. *In re Spada*, 911 F.2d 705, 708, 15 U.S.P.Q.2d 1655, 1657 (Fed. Cir. 1990); *Crown Operations Int'l, Ltd. v. Solutia Inc.*, 289 F.3d 1367, 1375, 62 U.S.P.Q.2d 1917, 1921 (Fed. Cir. 2002). The standard for an anticipatory reference is set forth in *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987): "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *See also Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 U.S.P.Q.2d 1913, 1920 (Fed. Cir. 1989) (holding that "[t]he identical invention must be shown in as complete detail as is contained in the...claim"). Further, the anticipating reference must disclose every element of the challenged claim and enable one skilled in the art to make the anticipating subject matter. *PPG Indus., Inc. v. Guardian Indus. Corp.* 75 F. 3d 1558, 1564, 37 U.S.P.Q.2d 1618, 1623 (Fed. Cir. 1996).

It is well established that in order for a prior art reference to amount to an inherent anticipation of a claim, all the elements of the claim must *necessarily*, *inevitably*, and *always* result from the prior art disclosure and would be so recognized by one of ordinary skill in the art; mere possibilities or probabilities are not sufficient. *See Continental Can Co. USA v. Monsanto Co.*, 948 F.2d 1264, 1269, 20 U.S.P.Q.2d 1746, 1749 (Fed. Cir. 1991). As stated by the Court of Appeals for the Federal Circuit:

> we are not persuaded that the 'effect' of the processes disclosed in [the prior art patents], an 'effect' undisclosed in those patents, would be always to inherently produce or be seen always to produce products meeting all of the claim limitations. Anticipation of inventions set forth in product claims cannot be predicated on mere conjecture respecting the characteristics of products that might result from the practice of processes disclosed in references.

W.L. Gore & Assocs., Inc. v. Garlock, Inc., 721 F.2d 1540, 1553-1554, 220 U.S.P.Q. 303, 313-314 (Fed. Cir. 1983) (citing *In re Felton*, 484 F.2d 495, 500, 179 U.S.P.Q. 295, 298 (C.C.P.A. 1973)).

It is not sufficient that a teaching of a prior art reference *could* yield a result that would anticipate the claim against which the prior art reference is applied; instead, to be anticipatory under the doctrine of inherency, the teaching of the prior art reference *must inevitably* lead to the result. As has also been stated:

> Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing *may* result from a given set of circumstances is not sufficient.

In re Oelrich, 666 F.2d 578, 581, 212 U.S.P.Q. 323, 325-26 (C.C.P.A. 1981) (citing *Hansgirg v. Kemmer*, 102 F.2d 212, 214, 40 U.S.P.Q. 665, 667 (C.C.P.A. 1939)).

2. <u>The Claims Are Not Anticipated By Abatangelo</u>

As a preliminary matter, Applicant submits that the rejected claims are not product-by-process claims; thus, the Examiner's statements regarding the patentability of a product not being dependent on its method of production are irrelevant. The recitation "decellularized bone marrow extracellular matrix...produced *in vivo* in an animal" refers to a component of the claimed biocompatible material (*i.e.*, extracellular matrix that was produced

by bone marrow *in vivo* and subsequently decellularized), not how the claimed biocompatible material is prepared.

Even assuming that the Examiner's characterization of the rejected claims is correct, which it is not, as previously discussed in the Amendment Under 37 C.F.R. § 1.111 filed October 5, 2006 (see pages 7 and 8, incorporated by reference herein), and for reasons set forth below, Applicant submits that Abatangelo does not teach or suggest that decellularized bone marrow extracellular matrix ("ECM") produced *in vivo* in an animal, as recited in claim 50, is the same as or obvious in view of bone marrow ECM produced *in vitro*.

In fact, Abatangelo does not even teach or suggest ECM produced by bone marrow *in vivo* or *in vitro*. Rather, Abatangelo discloses ECM produced by (i) specific connective tissue cells that are partially or completely differentiated from stem cells isolated from bone marrow, or (ii) the specific mature connective tissue cells (see page 3, line 26, to page 4, line 2). Bone marrow contains, among other things, two types of stem cells that are immature and undifferentiated: (i) hematopoietic stem cells (HSCs), which give rise to all components of the immune and blood systems, including white blood cells (leukocytes), red blood cells (erythrocytes), and platelets (thrombocytes); and (ii) mesenchymal stem cells (MSCs), which give rise to cells of varied lineage, including bone (osteoblasts), cartilage (chondrocytes), muscle (myocytes), adipose (adipocytes) and neural tissues (see, *e.g.*, Lodie *et al.*, "Systematic analysis of reportedly distinct populations of multipotent bone marrow-derived stem cells reveals a lack of distinction," Tissue Eng. 2002 Oct;8(5):739-51 (hereinafter "Lodie"), page 739, sentence bridging columns 1 and 2; and Pittenger *et al.*, "Multilineage potential of adult human mesenchymal stem cells," Science 1999 Apr 2;284(5411):143-47 (hereinafter "Pittenger"), page 143, col. 2, lines 10-18, made of record as references C35 and C36, respectively, in the Supplemental Information Disclosure Statement submitted herewith). In contrast, the connective tissue cells disclosed in Abatangelo are either mature or derived from partially/completely differentiated stem cells that have been isolated from bone marrow. Mature or partially/completely differentiated MSCs, such as osteoblasts, chondrocytes, myocytes, adipocytes, and nerve cells express cell type-specific markers such as alkaline phosphatase, type II collagen, desmin, peroxisome proliferation-activated receptor $\gamma 2$ (PPAR$\gamma 2$), and β-tubulin, respectively (see Lodie, Abstract, lines 15-17; page 746, col. 1, ¶1, lines 2-3; page 746, col. 1, ¶2, lines 1-2; page 748, col. 2, ¶2, lines 3-5; and page 750, col. 1, ¶2; and Pittenger, page 144, paragraph bridging columns 2 and 3; page 144, col. 3, ¶2; and

page 145, col. 1, ¶1). Thus, these connective tissue cells are different from the isolated stem cells from which they are differentiated, as well as different from the bone marrow that contained the stem cells. A person skilled in the art would understand that different cell populations produce different ECM, and thus, ECM produced by mature or partially/completely differentiated stem cells isolated from bone marrow (*e.g.*, the connective tissue cells of Abatangelo) would be different from ECM produced by the bone marrow of the presently claimed invention, which includes undifferentiated, non-isolated stem cells as well as other constituents..

Moreover, the production of bone marrow ECM depends on complex cellular interactions within a hematopoietic microenvironment that "consists of an organized array of endothelial cells lining the marrow vasculature with a network of fibroblasts, adventitial reticular cells, macrophages, and adipocytes in the hematopoietic cords" (see, *e.g.*, Paul *et al.*, 1991, "Stromal Cell-Associated Hematopoiesis: Immortalization and Characterization of a Primate Bone Marrow-Derived Stromal Cell Line," Blood, 77(8):1723-33, at page 1723, col. 1, ¶1, made of record as reference C37 in the Supplemental Information Disclosure Statement submitted herewith). The hematopoietic microenvironment in which bone marrow ECM is produced *in vivo* involves many different cells and the resulting cellular interaction between the many different cells. In contrast, Abatangelo only discloses the ECM produced from one type of connective tissue cell. Thus, the ECM produced by the connective tissue cells in Abatangelo is different from the bone marrow ECM produced *in vivo*.

For the foregoing reasons, Applicant submits Abatangelo does not disclose or suggest the ECM produced by bone marrow *in vivo*, as recited in claim 50. Thus, claim 50, and its dependent claims, are not anticipated by Abatangelo. Withdrawal of the rejection is respectfully requested.

II. THE CLAIM REJECTIONS UNDER 35 U.S.C. § 103 SHOULD BE WITHDRAWN

Claims 50-63 and 65 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Abatangelo in view of Cobb *et al.* (U.S. Patent 6,241,981, "Cobb"). Specifically, the Examiner alleges that while Abatangelo does not teach the composition further comprising vascular endothelial growth factor (VEGF), "[a]t the time of the claimed invention, VEGF was known and used in the art with tissue grafts" (see Office Action, page 5, ¶2), and "one of ordinary skill in the art would have recognized that the mixture of

Abatangelo could be used with any cell type for tissue grafts, and any corresponding growth factor." (see Office Action, page 6, ¶1). For the following reasons, Applicant respectfully disagrees.

1. The Legal Standard

A finding of obviousness under 35 U.S.C. § 103 requires a determination of the scope and the content of the prior art, the differences between the invention and the prior art, the level of the ordinary skill in the art, and whether the differences are such that the claimed subject matter as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made. *Graham v. Deere*, 383 U.S. 1 (1966). The relevant inquiry is whether the prior art suggests the invention, and whether one of ordinary skill in the art would have had a reasonable expectation that the claimed invention would be successful. *In re O'Farrell*, 853 F.2d 894, 902-4 (Fed. Cir. 1988); *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991). Both the suggestion of the claimed invention and the expectation of success must be in the prior art, not in the disclosure of the claimed invention. *In re Dow Chemical Co.*, 5 U.S.P.Q.2d 1529 (Fed. Cir. 1988). In determining obviousness, "the inquiry is not whether each element existed in prior art, but whether the prior art made obvious the invention as a whole for which patentability is claimed." *Hartness Int'l Inc. v. Simplimatic Eng'g Co.*, 819 F.2d 1100, 2 U.S.P.Q.2d 1826 (Fed. Cir. 1987). An analysis under 35 U.S.C. § 103(a) "should be made explicit," and "it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. __, 2007 WL 1237834, at *14 and *15, respectively (2007).

2. The Claims Are Not Obvious In View Of The References

As discussed above, Abatangelo does not teach or suggest bone marrow ECM, much less teach or suggest bone marrow ECM produced *in vivo*. In fact, Abatangelo teaches away from using unmodified bone marrow (as if *in vivo*) to produce ECM, since its methods require, *inter alia*, growing connective tissue cells from partially/completely differentiated stem cells isolated from bone marrow in a culture medium containing a differentiating factor such that the desired connective tissue cells are produced (see page 4, lines 18-23).

Cobb does not cure the deficiencies of Abatangelo. Cobb discloses tissue graft constructs for repairing neurological tissue (see Abstract). Cobb never mentions bone marrow, much less teach or suggest decellularized bone marrow ECM produced *in vivo* and being in the form of a scaffold. Accordingly, the combination of Abatangelo plus Cobb, even assuming there is motivation to combine the teachings of the two references, which there is none, does not suggest the presently claimed invention.

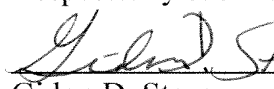
In view of the foregoing, Applicant respectfully submits that the rejection is in error and should be withdrawn.

CONCLUSION

Applicant respectfully requests entry of the remarks made herein into the file history of the present application. Withdrawal of the Examiner's rejections and an allowance of the application are earnestly requested. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

Respectfully submitted,

Date: June 4, 2007



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Gidon D. Stern (Reg. No.)

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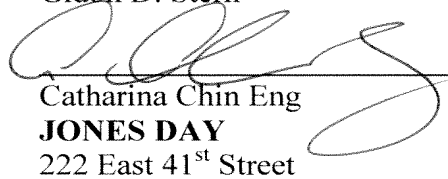

42,412
Catharina Chin Eng (Reg. No.)

JONES DAY
222 East 41st Street
New York, New York 10017
(212) 326-3939

Enclosures